

SEQUENCE LISTING

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SmithKline Beecham Biologicals S. A.

<120> HER-2/neu Fusion Proteins

<130> 014058-009810PC

<140> US 09/493,480
<141> 2000-01-28

<150> US 60/117,976
<151> 1999-01-29

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<170> PatentIn Ver. 2.1

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<212> PRT
<213> Homo sapiens

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<222> (1)..(653)
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<223> fragment of the phosphorylation domain, preferred portion (delta PD)

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Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Tyr Asp Met Lys
20 25 30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45

Express Mail No.
EL 827035155 US

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
 50 55 60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
 65 70 75 80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
 85 90 95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
 100 105 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
 115 120 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
 130 135 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
 145 150 155 160

Leu Cys Tyr Gln Asp Thr-Ile Leu Trp Lys Asp Ile Phe His Lys Asn
 165 170 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
 180 185 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
 195 200 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
 210 215 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
 225 230 235 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
 245 250 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
 260 265 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
 275 280 285

Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
 290 295 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
 305 310 315 320

Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
 325 330 335

Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
 340 345 350

Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
 355 360 365

Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
 370 375 380

Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
 385 390 395 400

Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
 405 410 415

Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
 420 425 430

Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
 435 440 445

Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
 450 455 460

Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
 465 470 475 480

Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
 485 490 495

Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
 500 505 510

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
 515 520 525

Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
 530 535 540

Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
 545 550 555 560

Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
 565 570 575

Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
 580 585 590

Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
 595 600 605

Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
 610 615 620

Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
 625 630 635 640

Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser
 645 650 655

Ala Val Val Gly Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly
 660 665 670

Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg
 675 680 685

Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly
 690 695 700
 Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu
 705 710 715 720
 Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys
 725 730 735
 Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile
 740 745 750
 Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu
 755 760 765
 Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg
 770 775 780
 Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu
 785 790 795 800
 Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg
 805 810 815
 Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly
 820 825 830
 Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala
 835 840 845
 Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe
 850 855 860
 Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp
 865 870 875 880
 Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg
 885 890 895
 Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val
 900 905 910
 Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala
 915 920 925
 Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro
 930 935 940
 Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met
 945 950 955 960
 Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe
 965 970 975
 Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu
 980 985 990
 Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu
 995 1000 1005

Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu
1010 1015 1020

Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly
1025 1030 1035 1040

Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly
1045 1050 1055

Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Ala Pro Arg
1060 1065 1070

Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp Gly
1075 1080 1085

Asp Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His
1090 1095 1100

Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu
1105 1110 1115 1120

Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln
1125 1130 1135

Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro
1140 1145 1150

Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu
1155 1160 1165

Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val
1170 1175 1180

Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln
1185 1190 1195 1200

Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala
1205 1210 1215

Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala
1220 1225 1230

Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr
1235 1240 1245

Leu Gly Leu Asp Val Pro Val
1250 1255

<210> 2
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<212> PRT
<213> Rattus sp.

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<223> rat HER-2/neu protein

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<223> extracellular domain (ECD)

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<223> intracellular domain (ICD)

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<221> DOMAIN
<222> (721)..(998)
<223> kinase domain (KD)

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<222> (991)..(1256)
<223> phosphorylation domain (PD)

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<222> (991)..(1049)
<223> fragment of the phosphorylation domain, preferred
      portion (delta PD)

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Pro Pro Gly Ile Ala Gly Thr Gln Val Cys Thr Gly Thr Asp Met Lys
  20          25           30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
  35          40           45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
  50          55           60

Val Pro Ala Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
  65          70           75           80

Gln Gly Tyr Met Leu Ile Ala His Asn Gln Val Lys Arg Val Pro Leu
  85          90           95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr
 100         105          110

Ala Leu Ala Val Leu Asp Asn Arg Asp Pro Gln Asp Asn Val Ala Ala
115          120          125

Ser Thr Pro Gly Arg Thr Pro Glu Gly Leu Arg Glu Leu Gln Leu Arg
130          135          140

Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Arg Gly Asn Pro
145          150          155          160

Gln Leu Cys Tyr Gln Asp Met Val Leu Trp Lys Asp Val Phe Arg Lys
165          170          175

Asn Asn Gln Leu Ala Pro Val Asp Ile Asp Thr Asn Arg Ser Arg Ala
180          185          190

Cys Pro Pro Cys Ala Pro Ala Cys Lys Asp Asn His Cys Trp Gly Glu
195          200          205

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Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile Cys Thr Ser Gly
210 215 220

Cys Ala Arg Cys Lys Gly Arg Leu Pro Thr Asp Cys Cys His Glu Gln
225 230 235 240

Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys
245 250 255

Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu
260 265 270

Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met His Asn Pro Glu Gly
275 280 285

Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Thr Cys Pro Tyr Asn Tyr
290 295 300

Leu Ser Thr Glu Val Gly Ser Cys Thr Leu Val Cys Pro Pro Asn Asn
305 310 315 320

Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser
325 330 335

Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg
340 345 350

Gly Ala Arg Ala Ile Thr Ser Asp Asn Val Gln Glu Phe Asp Gly Cys
355 360 365

Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly
370 375 380

Asp Pro Ser Ser Gly Ile Ala Pro Leu Arg Pro Glu Gln Leu Gln Val
385 390 395 400

Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp
405 410 415

Pro Asp Ser Leu Arg Asp Leu Ser Val Phe Gln Asn Leu Arg Ile Ile
420 425 430

Arg Gly Arg Ile Leu His Asp Gly Ala Tyr Ser Leu Thr Leu Gln Gly
435 440 445

Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser
450 455 460

Gly Leu Ala Leu Ile His Arg Asn Ala His Leu Cys Phe Val His Thr
465 470 475 480

Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His
485 490 495

Ser Gly Asn Arg Pro Glu Glu Asp Cys Gly Leu Glu Gly Leu Val Cys
500 505 510

Asn Ser Leu Cys Ala His Gly His Cys Trp Gly Pro Gly Pro Thr Gln
515 520 525

Cys Val Asn Cys Ser His Phe Leu Arg Gly Gln Glu Cys Val Glu Glu
530 535 540

Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Ser Asp Lys Arg
545 550 555 560

Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr
565 570 575

Cys Phe Gly Ser Glu Ala Asp Gln Cys Ala Ala Cys Ala His Tyr Lys
580 585 590

Asp Ser Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp
595 600 605

Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu Glu Gly Ile Cys
610 615 620

Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu
625 630 635 640

Arg Gly Cys Pro Ala Glu-Gln Arg Ala Ser Pro Val Thr Phe Ile Ile
645 650 655

Ala Thr Val Glu Gly Val Leu Leu Phe Leu Ile Leu Val Val Val Val
660 665 670

Gly Ile Leu Ile Lys Arg Arg Arg Gln Lys Ile Arg Lys Tyr Thr Met
675 680 685

Arg Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser
690 695 700

Gly Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu
705 710 715 720

Leu Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr
725 730 735

Lys Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala
740 745 750

Ile Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile
755 760 765

Leu Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser
770 775 780

Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln
785 790 795 800

Leu Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu His Arg Gly
805 810 815

Arg Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Val Gln Ile Ala Lys
820 825 830

Gly Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala
835 840 845

Ala Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp
850 855 860

Phe Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala
865 870 875 880

Asp Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu
885 890 895

Arg Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr
900 905 910

Val Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro
915 920 925

Ala Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln
930 935 940

Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp
945 950 955 960

Met Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu
965 970 975

Phe Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn
980 985 990

Glu Asp Leu Gly Pro Ser Ser Pro Met Asp Ser Thr Phe Tyr Arg Ser
995 1000 1005

Leu Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr
1010 1015 1020

Leu Val Pro Gln Gln Gly Phe Phe Ser Pro Asp Pro Thr Pro Gly Thr
1025 1030 1035 1040

Gly Ser Thr Ala His Arg Arg His Arg Ser Ser Ser Thr Arg Ser Gly
1045 1050 1055

Gly Gly Glu Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Gly Pro Pro
1060 1065 1070

Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp
1075 1080 1085

Gly Asp Leu Ala Met Gly Val Thr Lys Gly Leu Gln Ser Leu Ser Pro
1090 1095 1100

His Asp Leu Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Leu Pro
1105 1110 1115 1120

Leu Pro Pro Glu Thr Asp Gly Tyr Val Ala Pro Leu Ala Cys Ser Pro
1125 1130 1135

Gln Pro Glu Tyr Val Asn Gln Ser Glu Val Gln Pro Gln Pro Pro Leu
1140 1145 1150

Thr Pro Glu Gly Pro Leu Pro Pro Val Arg Pro Ala Gly Ala Thr Leu
1155 1160 1165

Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp
1170 1175 1180

Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Val Pro
1185 1190 1195 1200

Arg Glu Gly Thr Ala Ser Pro Pro His Pro Ser Pro Ala Phe Ser Pro
1205 1210 1215

Ala Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asn Ser Ser Glu Gln Gly
1220 1225 1230

Pro Pro Pro Ser Asn Phe Glu Gly Thr Pro Thr Ala Glu Asn Pro Glu
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Tyr Leu Gly Leu Asp Val Pro Val
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<212> PRT
<213> Homo sapiens

<220>
<223> extracellular domain (ECD) of human HER-2/neu

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Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20 25 30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100 105 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115 120 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130 135 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145 150 155 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165 170 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180 185 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195 200 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210 215 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225 230 235 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245 250 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260 265 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275 280 285

Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290 295 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305 310 315 320

Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
325 330 335

Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
340 345 350

Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
355 360 365

Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
370 375 380

Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385 390 395 400

Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
405 410 415

Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
420 425 430

Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
435 440 445

Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
450 455 460

Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465 470 475 480

Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
485 490 495

Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
500 505 510

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
515 520 525

Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
530 535 540

Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545 550 555 560

Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
565 570 575

Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
580 585 590

Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
595 600 605

Ser Tyr Met Pro Ile Trp-Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
610 615 620

Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
625 630 635 640

Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser
645 650

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<212> PRT
<213> Homo sapiens

<220>
<223> phosphorylation domain (PD) of human HER-2/neu

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Arg Ser Leu Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu
20 25 30

Glu Tyr Leu Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro
35 40 45

Gly Ala Gly Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg
50 55 60

Ser Gly Gly Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu
65 70 75 80

Ala Pro Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val
85 90 95

Phe Asp Gly Asp Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser Leu
100 105 110

Pro Thr His Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr
 115 120 125
 Val Pro Leu Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys
 130 135 140
 Ser Pro Gln Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro
 145 150 155 160
 Pro Ser Pro Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala
 165 170 175
 Thr Leu Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val
 180 185 190
 Lys Asp Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu
 195 200 205
 Thr Pro Gln Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe
 210 215 220
 Ser Pro Ala Phe Asp Asn-Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu
 225 230 235 240
 Arg Gly Ala Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn
 245 250 255
 Pro Glu Tyr Leu Gly Leu Asp Val Pro Val
 260 265

<210> 5
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 <212> PRT
 <213> Homo sapiens

<220>
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 portion (delta PD) of human HER-2/neu

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 Gln Asn Glu Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr
 1 5 10 15

Arg Ser Leu Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu
 20 25 30

Glu Tyr Leu Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro
 35 40 45

Gly Ala Gly Gly Met Val His His Arg His Arg
 50 55

<210> 6
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 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:fusion protein
of ECD and PD of human HER-2/neu

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Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20 25 30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100 105 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115 120 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130 135 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145 150 155 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165 170 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180 185 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195 200 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210 215 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225 230 235 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245 250 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260 265 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275 280 285

Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290 295 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305 310 315 320

Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
325 330 335

Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
340 345 350

Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
355 360 365

Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
370 375 380

Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385 390 395 400

Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
405 410 415

Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
420 425 430

Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
435 440 445

Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
450 455 460

Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465 470 475 480

Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
485 490 495

Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
500 505 510

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
515 520 525

Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
530 535 540

Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545 550 555 560

Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
565 570 575

Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
580 585 590

Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
595 600 605

Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
610 615 620

Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
625 630 635 640

Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Gln Asn Glu
645 650 655

Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu
660 665 670

Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu
675 680 685

Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly
690 695 700

Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly
705 710 715 720

Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Ala Pro Arg
725 730 735

Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp Gly
740 745 750

Asp Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His
755 760 765

Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu
770 775 780

Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln
785 790 795 800

Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro
805 810 815

Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu
820 825 830

Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val
835 840 845

Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln
850 855 860

Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala
865 870 875 880

Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala
885 890 895

Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr
900 905 910

Leu Gly Leu Asp Val Pro Val
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<211> 712
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:fusion protein
of ECD and delta PD of human HER-2/neu

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Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
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Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100 105 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115 120 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130 135 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145 150 155 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165 170 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180 185 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195 200 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210 215 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225 230 235 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245 250 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260 265 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
 275 280 285
 Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
 290 295 300
 Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
 305 310 315 320
 Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
 325 330 335
 Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
 340 345 350
 Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
 355 360 365
 Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
 370 375 380
 Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
 385 390 395 400
 Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
 405 410 415
 Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
 420 425 430
 Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
 435 440 445
 Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
 450 455 460
 Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
 465 470 475 480
 Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
 485 490 495
 Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
 500 505 510
 Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
 515 520 525
 Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
 530 535 540
 Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
 545 550 555 560
 Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
 565 570 575
 Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
 580 585 590

Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
595 600 605

Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
610 615 620

Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
625 630 635 640

Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Gln Asn Glu
645 650 655

Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu
660 665 670

Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu
675 680 685

Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly
690 695 700

Gly Met Val His His Arg His Arg
705 710

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<212> PRT
<213> Rattus sp.

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<223> extracellular domain (ECD) of rat HER-2/neu

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Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60

Val Pro Ala Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80

Gln Gly Tyr Met Leu Ile Ala His Asn Gln Val Lys Arg Val Pro Leu
85 90 95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr
100 105 110

Ala Leu Ala Val Leu Asp Asn Arg Asp Pro Gln Asp Asn Val Ala Ala
115 120 125

Ser Thr Pro Gly Arg Thr Pro Glu Gly Leu Arg Glu Leu Gln Leu Arg
130 135 140

Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Arg Gly Asn Pro
 145 150 155 160
 Gln Leu Cys Tyr Gln Asp Met Val Leu Trp Lys Asp Val Phe Arg Lys
 165 170 175
 Asn Asn Gln Leu Ala Pro Val Asp Ile Asp Thr Asn Arg Ser Arg Ala
 180 185 190
 Cys Pro Pro Cys Ala Pro Ala Cys Lys Asp Asn His Cys Trp Gly Glu
 195 200 205
 Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile Cys Thr Ser Gly
 210 215 220
 Cys Ala Arg Cys Lys Gly Arg Leu Pro Thr Asp Cys Cys His Glu Gln
 225 230 235 240
 Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys
 245 250 255
 Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu
 260 265 270
 Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met His Asn Pro Glu Gly
 275 280 285
 Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Thr Cys Pro Tyr Asn Tyr
 290 295 300
 Leu Ser Thr Glu Val Gly Ser Cys Thr Leu Val Cys Pro Pro Asn Asn
 305 310 315 320
 Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser
 325 330 335
 Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg
 340 345 350
 Gly Ala Arg Ala Ile Thr Ser Asp Asn Val Gln Glu Phe Asp Gly Cys
 355 360 365
 Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly
 370 375 380
 Asp Pro Ser Ser Gly Ile Ala Pro Leu Arg Pro Glu Gln Leu Gln Val
 385 390 395 400
 Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp
 405 410 415
 Pro Asp Ser Leu Arg Asp Leu Ser Val Phe Gln Asn Leu Arg Ile Ile
 420 425 430
 Arg Gly Arg Ile Leu His Asp Gly Ala Tyr Ser Leu Thr Leu Gln Gly
 435 440 445
 Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser
 450 455 460

Gly Leu Ala Leu Ile His Arg Asn Ala His Leu Cys Phe Val His Thr
 465 470 475 480
 Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His
 485 490 495
 Ser Gly Asn Arg Pro Glu Glu Asp Cys Gly Leu Glu Gly Leu Val Cys
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 Asn Ser Leu Cys Ala His Gly His Cys Trp Gly Pro Gly Pro Thr Gln
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 Cys Val Asn Cys Ser His Phe Leu Arg Gly Gln Glu Cys Val Glu Glu
 530 535 540
 Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Ser Asp Lys Arg
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 Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr
 565 570 575
 Cys Phe Gly Ser Glu Ala Asp Gln Cys Ala Ala Cys Ala His Tyr Lys
 580 585 590
 Asp Ser Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp
 595 600 605
 Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu Glu Gly Ile Cys
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 625 630 635 640
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 <213> Homo sapiens

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 <222> (2026)..(3765)
 <223> intracellular domain (ICD) of human HER-2/neu

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 <223> phosphorylation domain (PD) of human HER-2/neu

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 <223> preferred portion of the phosphorylation domain
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<211> 3955
<212> DNA
<213> *Rattus norvegicus*

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<223> rat HER-2/neu cDNA

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<222> (2057)..(3796)
<223> intracellular domain (ICD) of rat HER-2/neu

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<223> kinase domain (KD) of rat HER-2/neu

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<222> (2999)..(3796)
<223> phosphorylation domain (PD) of rat HER-2/neu

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<223> preferred portion of the phosphorylation domain
(delta PD) of rat HER-2/neu

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<211> 3771
<212> DNA
<213> Mus sp.

<220>
<223> mouse HER-2/neu

<400> 11

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<210> 12
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:5' primer for
mouse HER-2/neu amplification

<400> 12
ccatggagct ggccgcctgg tgccgttg 28

<210> 13
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:3' primer for
mouse HER-2/neu amplification

<400> 13
ggcccttctgg ttcatactgg cacatccagg c 31

<210> 14
<211> 1256
<212> PRT
<213> Mus sp.

<220>
<223> mouse HER-2/neu protein

<400> 14

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20 25 30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Pro | Ala | Asn | Ala | Ser | Leu | Ser | Phe | Leu | Gln | Asp | Ile | Gln | Glu | Val |
| 65 | | | | | | 70 | | | | 75 | | | | 80 | |
| Gln | Gly | Tyr | Met | Leu | Ile | Ala | His | Asn | Arg | Val | Lys | His | Val | Pro | Leu |
| | | | 85 | | | | | | 90 | | | | 95 | | |
| Gln | Arg | Leu | Arg | Ile | Val | Arg | Gly | Thr | Gln | Leu | Phe | Glu | Asp | Lys | Tyr |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Ala | Leu | Ala | Val | Leu | Asp | Asn | Arg | Asp | Pro | Leu | Asp | Asn | Val | Thr | Thr |
| | | | 115 | | | | | 120 | | | | | 125 | | |
| Ala | Ala | Pro | Gly | Arg | Thr | Pro | Glu | Gly | Leu | Arg | Glu | Leu | Gln | Leu | Arg |
| | | | 130 | | | | 135 | | | 140 | | | | | |
| Ser | Leu | Thr | Glu | Ile | Leu | Lys | Gly | Gly | Val | Leu | Ile | Arg | Gly | Asn | Pro |
| | | | 145 | | | | 150 | | | 155 | | | 160 | | |
| Gln | Leu | Cys | Tyr | Gln | Asp | Met | Val | Leu | Trp | Lys | Asp | Val | Leu | Arg | Lys |
| | | | 165 | | | | 170 | | | 175 | | | | | |
| Asn | Asn | Gln | Leu | Ala | Pro | Val | Asp | Met | Asp | Thr | Asn | Arg | Ser | Arg | Ala |
| | | | 180 | | | | 185 | | | 190 | | | | | |
| Cys | Pro | Pro | Cys | Ala | Pro | Thr | Cys | Lys | Asp | Asn | His | Cys | Trp | Gly | Glu |
| | | | 195 | | | | 200 | | | 205 | | | | | |
| Ser | Pro | Glu | Asp | Cys | Gln | Ile | Leu | Thr | Gly | Thr | Ile | Cys | Thr | Ser | Gly |
| | | | 210 | | | | 215 | | | 220 | | | | | |
| Cys | Ala | Arg | Cys | Lys | Gly | Arg | Leu | Pro | Thr | Asp | Cys | Cys | His | Glu | Gln |
| | | | 225 | | | | 230 | | | 235 | | | 240 | | |
| Cys | Ala | Ala | Gly | Cys | Thr | Gly | Pro | Lys | His | Ser | Asp | Cys | Leu | Ala | Cys |
| | | | 245 | | | | 250 | | | 255 | | | | | |
| Leu | His | Phe | Asn | His | Ser | Gly | Ile | Cys | Glu | Leu | His | Cys | Pro | Ala | Leu |
| | | | 260 | | | | 265 | | | 270 | | | | | |
| Ile | Thr | Tyr | Asn | Thr | Asp | Thr | Phe | Glu | Ser | Met | Leu | Asn | Pro | Glu | Gly |
| | | | 275 | | | | 280 | | | 285 | | | | | |
| Arg | Tyr | Thr | Phe | Gly | Ala | Ser | Cys | Val | Thr | Thr | Cys | Pro | Tyr | Asn | Tyr |
| | | | 290 | | | | 295 | | | 300 | | | | | |
| Leu | Ser | Thr | Glu | Val | Gly | Ser | Cys | Thr | Leu | Val | Cys | Pro | Pro | Asn | Asn |
| | | | 305 | | | | 310 | | | 315 | | | 320 | | |
| Gln | Glu | Val | Thr | Ala | Glu | Asp | Gly | Thr | Gln | Arg | Cys | Glu | Lys | Cys | Ser |
| | | | 325 | | | | 330 | | | 335 | | | | | |
| Lys | Pro | Cys | Ala | Gly | Val | Cys | Tyr | Gly | Leu | Gly | Met | Glu | His | Leu | Arg |
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| Gly | Ala | Arg | Ala | Ile | Thr | Ser | Asp | Asn | Ile | Gln | Glu | Phe | Ala | Gly | Cys |
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| Lys | Lys | Ile | Phe | Gly | Ser | Leu | Ala | Phe | Leu | Pro | Glu | Ser | Phe | Asp | Gly |
| | | | 370 | | | | 375 | | | 380 | | | | | |

Asn Pro Ser Ser Gly Val Ala Pro Leu Lys Pro Glu His Leu Gln Val
385 390 395 400

Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp
405 410 415

Pro Glu Ser Phe Gln Asp Leu Ser Val Phe Gln Asn Leu Arg Val Ile
420 425 430

Arg Gly Arg Ile Leu His Asp Gly Ala Tyr Ser Leu Thr Leu Gln Gly
435 440 445

Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser
450 455 460

Gly Leu Ala Leu Ile His Arg Asn Thr His Leu Cys Phe Val Asn Thr
465 470 475 480

Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His
485 490 495

Ser Gly Asn Arg Pro Glu Glu Ala Cys Gly Leu Glu Gly Leu Val Cys
500 505 510

Asn Ser Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln
515 520 525

Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu
530 535 540

Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Arg Gly Lys His
545 550 555 560

Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr
565 570 575

Cys Tyr Gly Ser Glu Ala Asp Gln Cys Glu Ala Cys Ala His Tyr Lys
580 585 590

Asp Ser Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp
595 600 605

Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu Glu Gly Ile Cys
610 615 620

Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu
625 630 635 640

Arg Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Val Thr Phe Ile Ile
645 650 655

Ala Thr Val Val Gly Val Leu Leu Phe Leu Ile Ile Val Val Val Ile
660 665 670

Gly Ile Leu Ile Lys Arg Arg Gln Lys Ile Arg Lys Tyr Thr Met
675 680 685

Arg Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser
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Gly Ala Val Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu
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 Lys Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala
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 Ile Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile
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 770 775 780
 Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln
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 Leu Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu His Arg Gly
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 Arg Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Val Gln Ile Ala Lys
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 Ala Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp
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 Phe Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala
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 Asp Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu
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 Arg Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr
 900 905 910
 Val Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro
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 Ala Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln
 930 935 940
 Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp
 945 950 955 960
 Met Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu
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 Phe Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn
 980 985 990
 Glu Asp Leu Gly Pro Ser Ser Pro Met Asp Ser Thr Phe Tyr Arg Ser
 995 1000 1005
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Leu Val Pro Gln Gln Gly Phe Phe Ser Pro Asp Pro Ala Leu Gly Thr
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Gly Ser Thr Ala His Arg Arg His Arg Ser Ser Ser Ala Arg Ser Gly
1045 1050 1055

Gly Gly Glu Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Pro Pro
1060 1065 1070

Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp
1075 1080 1085

Gly Asp Leu Ala Val Gly Val Thr Lys Gly Leu Gln Ser Leu Ser Pro
1090 1095 1100

His Asp Leu Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Leu Pro
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Leu Pro Pro Glu Thr Asp Gly Tyr Val Ala Pro Leu Ala Cys Ser Pro
1125 1130 1135

Gln Pro Glu Tyr Val Asn Gln Pro Glu Val Arg Pro Gln Ser Pro Leu
1140 1145 1150

Thr Pro Glu Gly Pro Pro Pro Ile Arg Pro Ala Gly Ala Thr Leu
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Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp
1170 1175 1180

Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Ala Pro
1185 1190 1195 1200

Arg Ala Gly Thr Ala Ser Gln Pro His Pro Ser Pro Ala Phe Ser Pro
1205 1210 1215

Ala Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asn Ser Ser Glu Gln Gly
1220 1225 1230

Pro Pro Pro Ser Thr Phe Glu Gly Thr Pro Thr Ala Glu Asn Pro Glu
1235 1240 1245

Tyr Leu Gly Leu Asp Val Pro Val
1250 1255

<210> 15
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:PCR primer
PDM-251

<400> 15
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32

<210> 16
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:PCR primer
PDM-279

<400> 16
ctggactcg a gtcattagcg g tgcctgtgg tgg 33

<210> 17
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:AW028 hECD-PD
sense primer with NcoI site

<400> 17
ggccatggg g a g c a c c a a g t g t g c a c c g g c 32

<210> 18
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:AW029 hECD-PD
antisense primer with XhoI site without stop

<400> 18
gggctcgagc a ctggcacgt c c a g a c c a g g 31

<210> 19
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:AW038 primer
for site-directed mutagenesis

<400> 19
ggccccatcca g c c c g a t g g a c a g c a c t t c t a c c g 35

<210> 20
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:AW039 primer
for site-directed mutagenesis

<400> 20
cggtagaagg tgctgtccat cgggctggag gggcc 35

<210> 21
<211> 28
<212> DNA
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<220>
<223> Description of Artificial Sequence:AW036 sense
primer with NcoI site

<400> 21
ggccatggg taccctaaatg tgtaaccgg 28

<210> 22
<211> 61
<212> DNA
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<220>
<223> Description of Artificial Sequence:AW037 antisense
primer with XhoI site

<400> 22
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<210> 23
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Ra12.JC05 PCR
fragment

<400> 23
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<210> 24
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Ra12.JC06 PCR
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<400> 24
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<210> 25
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:LeIF.JC03 PCR
fragment

<400> 25
cgcccatggc gcagaatgat aagatcgccc

30

<210> 26
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:LeIF.JC04 PCR
fragment

<400> 26
cccccatggc gtcgcgcatg aacttcttcg tc

32